Subcommittee on Health

Committee on Energy and Commerce

Project Bioshield Reauthorization Issues

Summary of Prepared Testimony:

Bruce Cohen, President and CEO, Cellerant Therapeutics, Inc.

Cellerant Therapeutics, Inc. has a preclinical product, CLT-008, that is being developed for civilian applications for the treatment of infections and neutropenia due to radiation therapy and chemotherapy. It also possesses characteristics that make it suitable as a treatment for Acute Radiation Syndrome after a nuclear terror incident:

- **It is a safe, universal, off-the-shelf cell based medicine;**
- **It can be stored frozen in the Strategic National Stockpile for at least 10 years;**
- **It can be deployed to the site of disaster in high density cold storage;**
- **It can be administered up to 7 days post-exposure and still be effective; and**
- **It can be easily administered to patients by intravenous infusion.**

Cellerant has received some modest NIH grant funding to support the development of CLT-008 for biodefense, but has identified three major issues with the current implementation of Bioshield:

(1) **Project Bioshield (current law) does not provide specific funding mechanisms for scale up, process development and clinical trials.**

(2) **The current system does not provide sufficient incentives for small, private companies and seems to favor large corporations.**

(3) **Current law does not encourage innovation.**

Cellerant suggests the following solutions:

(1) **Authorize funding, through an existing or new agency, to address pre-clinical scale up and cost reduction: the current "Valley of Death" for Bioshield product development.**

(2) **Authorize a new or existing agency to fund human safety trials for countermeasures being developed for Bioshield.**

(3) **Establish an improved formal mechanism, other than SBIR, for funding small companies engaged in biodefense research and product development.**

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Testimony of:

Bruce Cohen, President and CEO, Cellerant Therapeutics, Inc.

Good afternoon and thank you for the opportunity to testify before the Subcommittee today. My name is Bruce Cohen, and I am the President and Chief Executive Officer of Cellerant Therapeutics, Inc., a clinical stage biotechnology company developing adult stem cell based therapies for cancer, genetic blood disorders and autoimmune disease. I am presenting this testimony because one of our pre-clinical products is also being developed as a universal counter-measure to improve survival and treat Acute Radiation Syndrome resulting from a nuclear terror incident. While the devastation of such an attack is difficult to contemplate, it is incumbent upon us to develop strategies that can rescue as many victims as we possibly can.

Radiation is an important therapy in the treatment of various cancers. Doses of chemotherapy and radiation that damage the blood-forming and gastrointestinal systems are frequently employed in the treatment of cancers or preparation for hematopoietic cell transplantation. Our product, CLT-008, is a cultured myeloid progenitor cell product that we have developed to address a pressing need in medicine – patients with compromised immune systems as a result of chemotherapy and radiation treatments. Despite advances in medical care, these patients are highly vulnerable to infections and internal bleeding with a significant risk of mortality.

From a medical perspective, these patients are very much like those we would encounter in the aftermath of a nuclear terror incident such as an attack on a nuclear power plant or the detonation of a nuclear weapon smuggled in a container vessel. Much of what we know about the impact of radiation on civilian populations is based on our experience at Chernobyl. Depending upon the dose of radiation to which a person is exposed, a variety

of medical problems can ensue with serious organ involvement, described generally as Acute Radiation Syndrome, the precise manifestations of which will be highly variable and dependent on the nature of the exposure. The most therapeutically addressable manifestation of ARS is known as hematopoietic syndrome, in which the blood-forming and immune system is damaged. Following a nuclear terror incident, civilians and first responders would receive doses of radiation that would profoundly damage their blood-forming and immune systems to the extent that they would not be able to resist common infections or recover from internal bleeding. Even temporary failure of the blood-forming and immune system without adequate medical support can be lethal, especially in a mass casualty setting.

Our extensive studies in preclinical animal models of lethal irradiation have been published in peer-reviewed scientific journals and predict that our product, CLT-008, will be capable of rescuing a significant number of victims of nuclear terror. Our studies suggest that CLT-008 protects against lethal infections and can be administered 4-7 days after radiation exposure. Decades of clinical experience in cell cryopreservation and infusion predict that our product will be stable in frozen vials for as long as 10 years, making it suitable for inclusion in the Strategic National Stockpile. CLT-008 can be infused by any medical technician trained in the administration of intravenous infusions. Our product offers the potential for a bridging therapy, providing victims with temporary immune competence for 30-45 days, allowing them time to seek more durable treatments when the situation becomes more stable.

No other pharmaceutical product, whether approved or in development, is able to permanently or temporarily reconstitute the immune system to the degree necessary to rescue large numbers of civilians, first responders, or warfighters. Of the limited number of products proposed, most would have to be given before or immediately after exposure, something that is unlikely to be practical in the event of a catastrophic nuclear terror incident. Most medical experts agree that orally-available drugs are unlikely to be effective in restoring an immune system which has suffered profound damage from radiation. Cell-based medicines, like the one we have under development, hold the

promise of being able to rescue large numbers of otherwise lethally irradiated victims, in a timely manner and with the limited medical capabilities that are likely to be available in the aftermath of a nuclear terror event.

Our experience with the U.S. Government in developing this product as a counter-measure to nuclear terror has been mixed. We have been awarded modestly sized, peer-reviewed research grants from the NIH. However, we have been frustrated by the limitations of the current system in its ability to support the next stage of development – confirmation of safety and efficacy in humans. I would like to outline the limitations of the current system and suggest some alternatives.

(1) Project Bioshield (current law) does not provide specific funding mechanisms for scale up, process development and clinical trials.

While it is technically possible under existing law for the NIH to fund projects related to commercial scale-up, process development aimed at cost-reduction, and the initiation of human clinical trials, grant mechanisms to support this activity for private companies do not exist or are extremely limited in scope. The NIH peer-review grant process has been an extraordinary contributor to the advancement of science and medicine in the U.S., but it has not focused on translating those discoveries toward commercial applications in the private sector. For most medical products, this is appropriate, as the pharmaceutical industry, venture capital community and public investors have been able to make the necessary investments that have made the U.S. the world's leader in biotechnology. However, those sources of capital are not available for the development of medical products whose primary customer is the U.S. Government through Project Bioshield acquisition. Typical private investors will not assume the risk of doing business with the Government, specifically making a large investment in research without a firm commitment to make the contemplated purchase.

Since the current Bioshield program does not allow the Government to enter into contracts with companies until they have shown human safety and have a defined, and

cost-effective manufacturing process, companies like Cellerant find themselves in the Valley of Death. That is, we do not have adequate financial resources to move our pre-clinical programs aggressively into human clinical trials, but without the results of those trials, we cannot compete for contracts under Project Bioshield. In addition, to the extent we are developing novel agents that have not previously been manufactured, we are likely to have production economics that will make the purchase contract unattractive, either from the Government's perspective of total cost or the company's perspective of generating an adequate return on investor capital.

This Valley of Death funding gap means that, in our case, we have had to slow development of our product in accordance with our ability to raise venture capital based on a non-Government application of our technology. That funding is available, but it takes an enormous amount of time and effort, and our investors are not prepared to have us use their capital for a program whose financing is beyond the control of the commercial pharmaceutical market.

(2) The current system does not provide sufficient incentives for small, private companies and seems to favor large corporations.

The current Bioshield program is biased toward the purchase of products which have been developed and approved for other reasons and which are being re-directed toward biodefense countermeasures. For example, the currently pending Bioshield nuclear countermeasure acquisition offer from HHS requires that eligible contractors manufacture a minimum number of doses prior to being paid by the Government. That is practical for a product which already has a defined commercial market, since the inventory could be used for other purposes in the event the Government decides not to complete the purchase. For an innovative product like ours, which has higher manufacturing costs, the risk of producing a large lot with no guaranteed buyer is unacceptable. That risk may well be borne by a larger company with greater capital resources, but it discourages small companies from competing.

The irony of the current system that seems to favor large companies is this: for most large pharmaceutical companies, the economics and market potential associated with producing biodefense products do not justify the commitment of significant resources, because their investors are expecting the development of blockbuster products and do not value the financial impact of a Government contract. For emerging biotech companies, what appears to be a relatively small market to a larger company may well be considered a substantial business opportunity. In addition, investors in biotech companies highly value the award of even a modestly sized contract because it is significant relative to the company's cash requirements and because it is seen as a form of scientific validation. Small companies are also more efficient in developing innovative new medical therapies, particularly for specialty applications.

(3) Current law does not encourage innovation.

Innovation comes from taking a fresh look at a problem and leads to the development of novel entities. The current process unfortunately encourages derivative development, i.e., finding new uses for old inventions. Thus, it becomes quite practical for a company to identify a new indication for an established drug (e.g., Ciprofloxacin as a treatment for anthrax), but the current rules do not encourage small, innovative companies to challenge current thinking, create novel paradigms, and make therapeutic breakthroughs.

In our domain, adult-derived cell therapies, we have a very different approach to the development of medicines. Our products are based on human cells. The science behind our approach has been translated into clinical practice for more than 40 years with relatively low risk for toxicity. However, cell-based therapies uniformly incur high manufacturing costs since they are derived from human source material and must be processed in controlled environments. We do not enjoy conventional pharmaceutical economics where the cost of the product itself is relatively modest compared to the cost of research and development. Both (a) the inability of the Government to fund research related to cost-reducing the manufacture of cellular medicines and (b) the procurement policies related to the need to produce numbers of doses prior to getting paid make it very

difficult for innovative approaches to succeed. Successful translation of scientific innovations to protect us from the medical consequences of nuclear attack requires innovation in the funding mechanisms.

We believe that there are a number of solutions to the problems that we and others have encountered.

(1) The first solution would be to specifically authorize funding to address the Valley of Death. The Government, either through a new agency, the NIH, or HHS/Bioshield, should be able to enter into non-competitive contracts for the achievement of very specific tasks, relating to the nation's priorities in national defense, for pre-clinical scale up for promising products that have demonstrated potential based on peer-reviewed animal experiments. Competitive review is appropriate for early stage work, where it is not possible to determine the probability of success except with highly trained peer reviewers. However, the rigor of a well established academic and private sector peer-review process, as evidenced by publications in major journals or presentation at recognized national meetings, can be used to accelerate programs which have already demonstrated scientific and clinical merit. There is no need to delay the award of contracts for the achievement of very specific purposes by insisting on a prolonged scientific competition.

(2) The second solution would be to direct, not simply authorize, a new or existing agency to fund human safety trials for products being developed as priority biodefense countermeasures, particularly nuclear countermeasures. While such authority technically exists within current authorities throughout HHS and DOD, a Congressional mandate to address this key element of the Valley of Death would encourage innovation and ensure the participation of smaller companies. The Government could easily put into place the necessary controls and require the concurrence of the FDA as to the readiness of the product for human trials, a rigorous process that has served the industry and our country quite well.

(3) The third solution would be to establish an improved formal mechanism for funding small companies engaged in biodefense research and product development. The limitations with the current SBIR program, including the relatively low level of funding provided in the first year and the modest levels provided in additional years, make this program an inefficient and time-consuming mechanism for funding research to address urgent and potentially catastrophic terror events. One such option would be to provide promising technologies with multi-year commitments that would be subject to the completion of specific milestones, in much the same way as private investors commit capital contingent on technological achievements being met. This would make the grant programs more attractive because the promise of milestone-driven funding would then justify the expense and time associated with grant preparation, provided, of course, that the technology proved to be valuable.

Throughout the country, there are academic and commercial enterprises that have access to extraordinarily talented people and ideas. A modest investment by the Government, coupled with the relaxation of a few counter-productive restrictions would unleash this capacity and provide the nation with the ability to respond to an event of unimaginable consequences.

Thank you again for the opportunity to testify today. I would be pleased to answer any questions you may have.